

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

Appl. No. 09/526,437; Filed: March 15, 2000
Dkt. No. 1488.0710005; Group Art Unit: 1647
Inventor(s): Greene *et al.*; Tel: 202/371-2600
Title: Antibodies to Human Tumor Necrosis Factor Receptor-Like Genes

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10	30	50
CGCCCAGCCGCCGCTCCAAGCCCCTGAGGTTTCCGGGGACCACAATGAACAAGTTGCTG		
		M N K L L
70	90	110
TGCTGCGCGCTCGTGTTTCTGGACATCTCCATTAAGTGGACCACCCAGGAAACGTTTCTC		
C C A L V F L D I S I K W T T O E T F P		
130	150	170
CCAAAGTACCTTCAATATGACGAAGAACTCTCATCAGCTGTTGTGTGACAAATGTCCT		
P K Y L H Y D E E T S H Q L L C D K C P		
190	210	230
CCTGGTACCTACCTAAAACAACACTGTACAGCAAAGTGAAGACCGTGTGCCCCCTTGC		
P G T Y L K Q H C T A K W K T V C A P C		
250	270	290
CCTGACCACTACTACACAGACAGCTGGCACACCAGTGACGAGTGTCTATACTGCAGCCCC		
P D H Y Y T D S W H T S D E C L Y C S P		
310	330	350
GTGTGCAAGGAGCTGCAGTACGTCAAGCAGGAGTGCAATCGCACCCACAACCGGTGTGC		
V C K E L Q Y V K Q E C N R T H N R V C		
370	390	410
GAATGCAAGGAAGGGCGCTACCTTGAGATAGAGTTCTGCTTGAAACATAGGAGCTGCCCT		
E C K E G R Y L E I E F C L K H R S C P		
430	450	470
CCTGGATTGGAGTGGTGCAAGCTGGAACCCAGAGCGAAATACAGTTTGCAAAAGATGT		
P G F G V V Q A G T P E R N T V C K R C		
490	510	530
CCAGATGGGTCTTCTCAAATGAGACGTATCTAAAGCACCCCTGTAGAAAACACACAAAT		
P D G F F S N E T S S K A P C R K H T N		
550	570	590
TGCAGTGTCTTTGGTCTCCTGCTAACTCAGAAAGGAAATGCAACACACGACAACATATGT		
C S V F G L L L T Q K G N A T H D N I C		
610	630	650
TCCGGAACAGTGAATCAACTCAAAAATGTGGAATAGATGTTACCCTGTGTGAGGAGGCA		
S G N S E S T Q K C G I D V T L C E E A		
670	690	710
TTCTTCAGGTTTGCTGTTTCTACAAAGTTTACGCCTAACTGGCTTAGTGTCTTGGTAGAC		
F F R F A V P T K F T P N W L S V L V D		
730	750	770
AATTTGCCTGGCACCAAAGTAAACGCAGAGAGTGTAGAGAGGATAAAACGGCAACACAGC		
N L P G T K V N A E S V E R I K R Q H S		
790	810	830
TCACAAGAACAGACTTTCCAGCTGCTGAAGTTATGGAACATCAAAACAAAGACCAAGAT		
S Q E Q T F Q L L K L W K H Q N K D Q D		

FIG. 1A

APPROVED	D.G. FIG.	
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 Title: Antibodies to Human Tumor Necrosis Factor Receptor-
 Like Genes

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```

      850              870              890
ATAGTCAAGAAGATCATCCAAGATATTGACCTCTGTGAAAACAGCGTGCAGCGGCACATT
I V K K I I Q D I D L C E N S V Q R H I
      910              930              950
GGACATGCTAACCTCACCTTCGAGCAGCTTCGTAGCTTGATGGAAAGCTTACCGGGAAG
G H A N L T F E Q L R S L M E S L P G K
      970              990              1010
AAAGTGGGAGCAGAAGACATTGAAAAACAATAAAGGCATGCAAACCCAGTGACCAGATC
K V G A E D I E K T I K A C K P S D Q I
      1030             1050             1070
CTGAAGCTGCTCAGTTTGTGCCGAATAAAAAATGGCGACCAAGACACCTTGAAGGGCCTA
L K L L S L W R I K N G D Q D T L K G L
      1090             1110             1130
ATGCACGCACTAAAGCACTCAAAGACGTACCACTTCCCAAACTGTCACTCAGAGTCTA

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FIG.1A1

APPROVED	O.G. FIG.	
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 Like Genes

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```

M H A L K H S K T Y H F P K T V T Q S L
1150                      1170                      1190
AAGAAGACCATCAGGTTCCCTTCACAGCTTCACAATGTACAAATTGTATCAGAAGTTATTT
K K T I R F L H S F T M Y K L Y Q K L F
1210                      1230                      1250
TTAGAAATGATAGGTAACCAGGTCCAATCAGTAAAAATAAGCTGCTTATAACTGGAAATG
L E M I G N Q V Q S V K I S C L *
1270                      1290                      1310
GCCATTGAGCTGTTTCCTCACAATTGCCGAGATCCCATGGATGAGTAAACTGTTTCTCAG
1330                      1350                      1370
GCACCTGAGGCTTTCAGTGATATCTTTCTCATTACCAGTGACTAATTTTGCCACAGGGTA
1390                      1410                      1430
CTAAAAGAACTATGATGTGGAGAAAGGACTAACATCTCCTCCAATAAACCCCAAATGGT
1450                      1470                      1490
TAATCCAACGTCAGATCTGGATCGTTATCTACTGACTATATTTTCCCTTATTACTGCTT
1510
GCAGTAATTCAACTCGAAAAAAAAAAAAA

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FIG.1B

APPROVED	O.G. FIG.	
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Title: Antibodies to Human Tumor Necrosis Factor Receptor-Like Genes

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```

      10              30              50
ATGAACAAGTTGCTGTGCTGCGCGCTCGTGTCTTCTGGACATCTCCATTAAGTGGACCACC
M N K L L C C A L V F L D I S I K W T T
      70              90              110
CAGGAAACGTTTCTCCTCAAAGTACCTTCATTATGACGAAGAAACCTCTCATCAGCTGTTG
Q E T F P P K Y L H Y D E E T S H Q L L
      130             150             170
TGTGACAAATGTCTCCTGGTACCTACCTAAAAACAACACTGTACAGCAAAGTGAAGACC
C D K C P P G T Y L K Q H C T A K W K T
      190             210             230
GTGTGCGCCCTTGGCCCTGACCACTACTACACAGACAGCTGGCACACCAGTGACGAGTGT
V C A P C P D H Y Y T D S W H T S D E C
      250             270             290
CTATACTGCAGCCCCGTGTGCAAGGAGCTGCAGTACGTCAAGCAGGAGTGCAATCGCACC
L Y C S P V C K E L Q Y V K Q E C N R T
      310             330             350
CACAACCGCGTGTGCGAATGCAAGGAAGGGCGCTACCTTGAGATAGAGTTCTGCTTGAAA
H N R V C E C K E G R Y L E I E F C L K
      370             390             410
CATAGGAGCTGCCCTCCTGGATTGGAGTGGTGCAAGCTGGAACCCAGAGCGGAAATACA
H R S C P P G F G V V Q A G T P E R N T
      430             450             470
GTTTGCAAAAGATGTCCAGATGGGTCTTCTCAAATGAGACGTCATCTAAAGCACCTGT
V C K R C P D G F F S N E T S S K A P C
      490             510             530
AGAAAAACACACAAATTGCAGTGTCTTTGGTCTCCTGCTAACTCAGAAAGGAAATGCAACA
R K H T N C S V F G L L L T Q K G N A T
      550             570             590
CACGACAACATATGTTCCGGAACAGTGAATCAACTCAAAAATGTGGAATAGATGTTACC
H D N I C S G N S E S T Q K C G I D V T
      610             630             650
CTGTGTGAGGAGGCATTCTTCAGGTTTGTGTTCTACAAAGTTTACGCCTAACTGGCTT
L C E E A F F R F A V P T K F T P N W L
      670             690             710
AGTGTCTTGGTAGACAATTTGCCTGCCACCAAAGTAAACGCAGAGAGTGTAGAGAGGATA
S V L V D N L P G T K V N A E S V E R I
      730             750             770
AAACGGCAACACAGCTCACAAGAACAGACTTTCCAGCTGCTGAAGTTATGAAACATCAA
K R Q H S S Q E Q T F Q L L K L W K H Q
      790             810             830
AACAAAGACCAAGATATAGTCAAGAAGATCATCCAAGATATTGACCTCTGTGAAAACAGC
N K D Q D I V K K I I Q D I D L C E N S

```

FIG.2A

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
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```

      850              870              890
GTGCAGCGGCACATTGGACATGCTAACCTCACCTTCGAGCAGCTTCGTAGCTTGATGGAA

V  Q  R  H  I  G  H  A  N  L  T  F  E  Q  L  R  S  L  M  E
      910              930              950
AGCTTACCGGGAAGAAAGTGGGAGCAGAAGACATTGAAAAACAATAAAGGCATGCAAAA
S  L  P  G  K  K  V  G  A  E  D  I  E  K  T  I  K  A  C  K
      970              990              1010
CCCAGTGACCAGATCCTGAAGCTGCTCAGTTTGTGGCGAATAAAAAATGGCGACCAAGAC
P  S  D  Q  I  L  K  L  L  S  L  W  R  I  K  N  G  D  Q  D
      1030             1050             1070
ACCTTGAAGGGCCTAATGCACGCACTAAAGCACTCAAAGACGTACCACITTCCTCCAAACT
T  L  K  G  L  M  H  A  L  K  H  S  K  T  Y  H  F  P  K  T
      1090             1110             1130
GTCACCTCAGAGTCTAAAGAAGACCATCAGGTTCCCTTCACAGCTTCACAATGTACAAATTG
V  T  Q  S  L  K  K  T  I  R  F  L  H  S  F  T  M  Y  K  L
      1150             1170

```

FIG.2A1

```

TATCAGAAGTTATTTTTAGAAATGATAGGTAATCTAGAAAAGATCTAA
Y  Q  K  L  F  L  E  M  I  G  N  L  E  K  I

```

FIG.2B

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Like Genes

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1MNKLLCCALVFLDISIKWTTQETFPF.....KYLHYDEETS 36
: |.:| :. . :.| .|. | :. . | :|.
1 MAPVAVWAALAVGLELWAAAHALPAQVAFTPYAPEPGSTCRLREYYDQTA 50
37 HQLLCDKCPPGTYLKQHCTAKWKTVCAPCPDHYYTDSWHTSDECLYCSPV 86
|:|.|||.|||. | || ...|||.|. | ||: |:|. ||| |:.
51 .QMCCSKCSPGQHAQVFKTKTSDTVCDSCEDSTYQLWNWVPECLSCGSR 99
87 CKELQYVKQECNRTHNRVCECKEGRYLEIE.....FCLKHRSCPPGFGV 130
|.. | .|.|.|.||:|. |:|. |:| :. :| .|.|.||||
100 CSSDQVETQACTREQNRICTCRPGWYCALSKQEGCRLCAPLRKCRPGFGV 149
131 VQAGTPERNTVCKRCPDGGFFSNETSSKAPCRKHTNCSVFGLLLTKGNAT 180
...:|...:|...|.:.| |||.|||. . |||. | .|.:. . |||. .
150 ARPGTETSDVVKPCAPGTFSTNTSSTDICRPHQICNVVAI....PGNAS 195
181 HDNIC.....SGNSESTQKCGIDVTLCEEAFF... 207
|.:| |.:|: ||... ||:
196 MDAVCTSTSPTRSMAPGAVHLPQPVSTRSQHTQPTPEPSTAPSTSFLPM 245
208RF AVPTKFIPNWL SVLVDNLPGTKVNAESVERIKR.... 242
||:|. :... . :| . ||. :.:|:
246 GPSPPAEGSTGDFALPVGLIVG..VTALGLLIIGVVNCVIMTQVKKKPLC 293
243 .QHSSQEQTFLLLKWKHQNKDQDIV....KKIIQDIDLCENSVQRHIG 286
|:.... :. | : |.:|: : .. :.: :.:|: .
294 LQREAKVPHLPADKARGTQGPEQQHLLITAPSSSSSSLESSASALDRRAP 343
287 HANLTFEQLRSLMESLPGK...KVGAEIEKTIKACKPSDQILKLLSLWR 333
| . | .: . | :| . .|. | : : : .
344 TRNQP..QAPGVEASGAGEARASTGSSDSSPGGHGTQVNVTCIVNVCSSS 391
334 IKNGDQDTLKGLMHALKHKSITYHFPKTVTQSLKKTIRFLHS....FTMY 378
.: : : :. |. . ||. :. | . :| | :.
392 DHSSQCSSQASSTMGDTDSSPSESPKDEQVPFSKEECAFRSQLETPETLL 441
379 KLYQKLFLEMIGNQVQSVKISCL. 401
:. |.: | . :.:| | |
442 GSTEEKPLPL.GVPDAGMKPS... 461

FIG. 3

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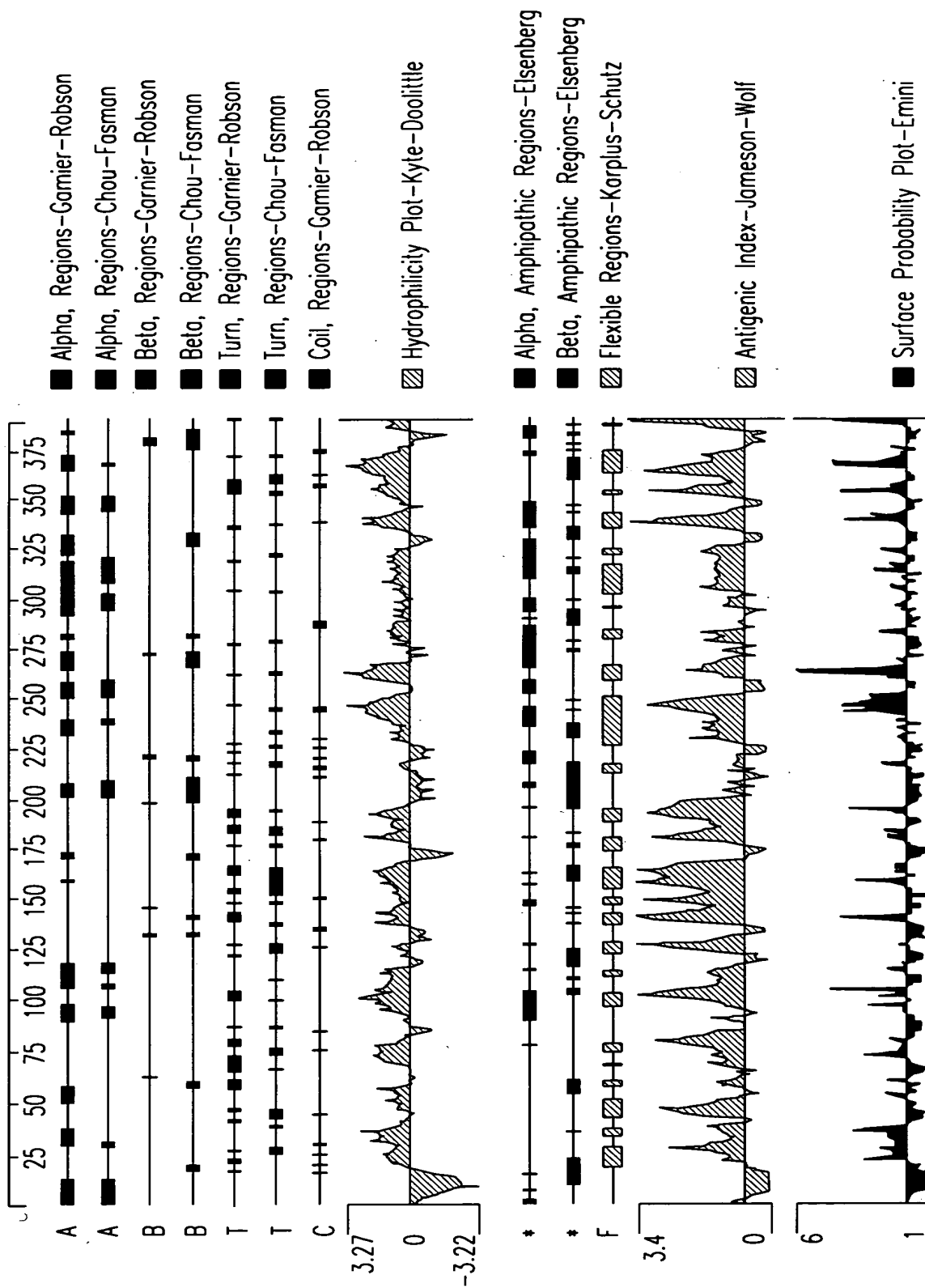


FIG. 4

APPROVED	D.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

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GOAT ANTI-HUMAN sTNFR I HAS CROSS-REACTIVITY
TO HSABH13

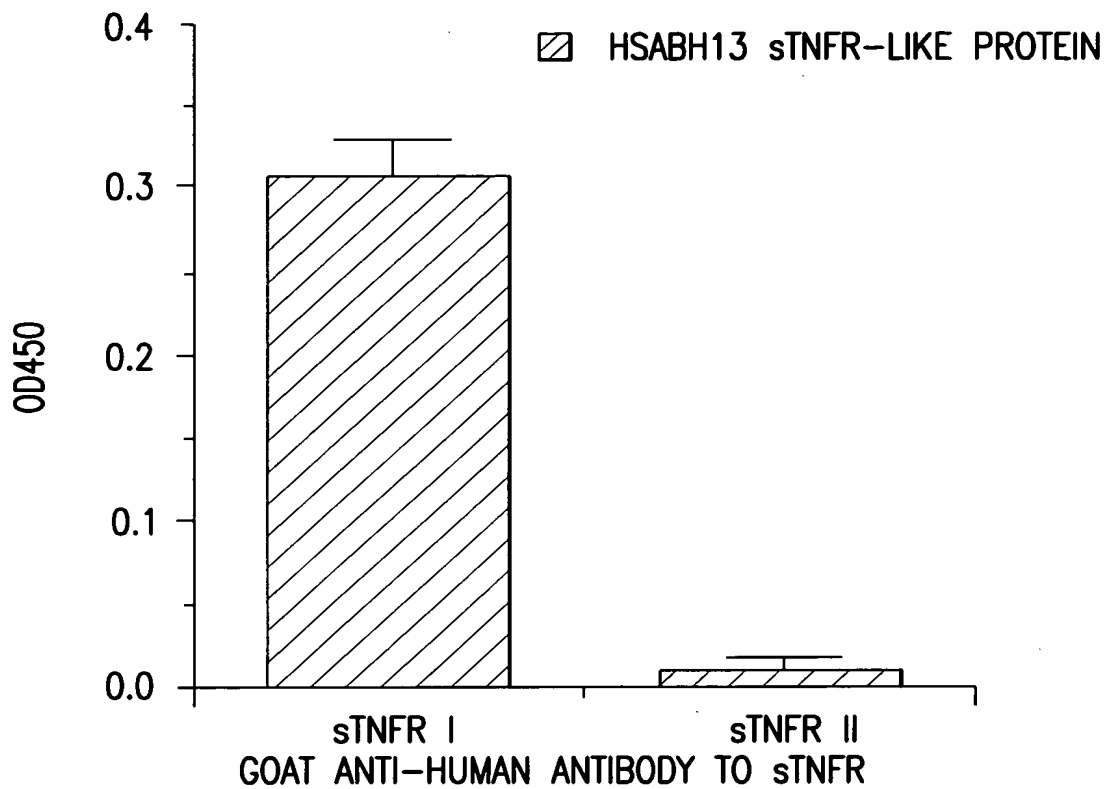


FIG.5

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

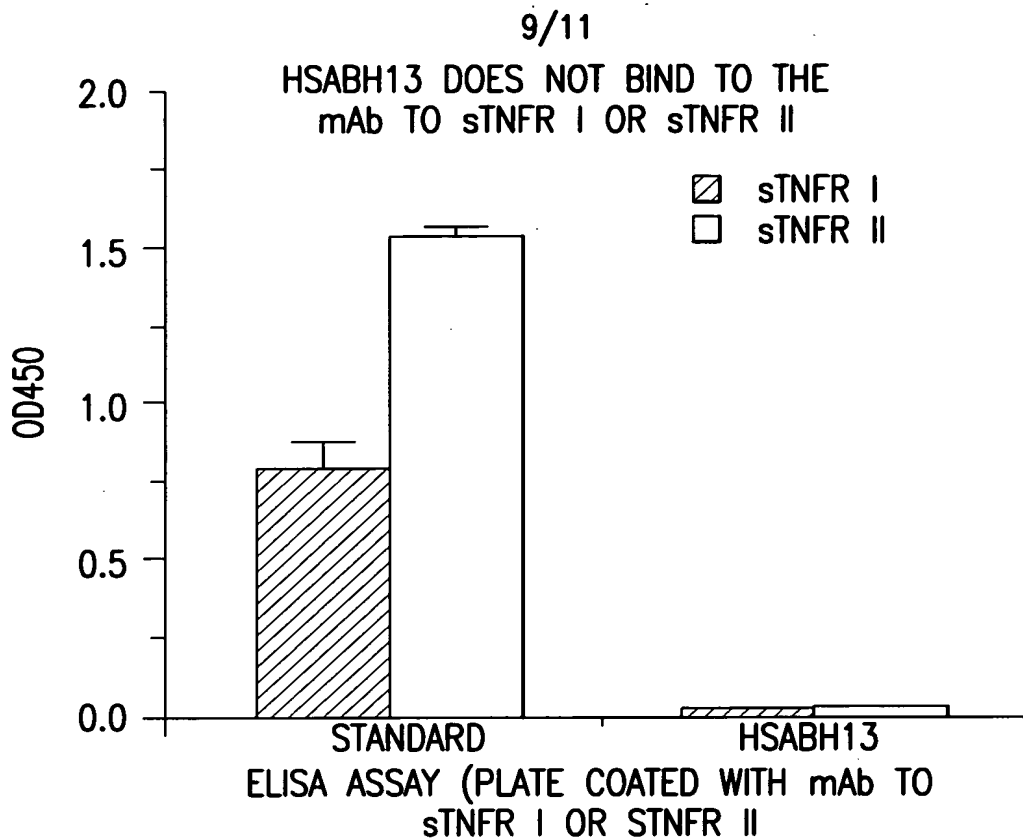


FIG.6

**TNF-BETA HAS HIGHER AFFINITY TO HSAHAB13 THAN TNF-ALPHA,
AND HUVE019 DOES NOT INHIBIT THE BINDING**

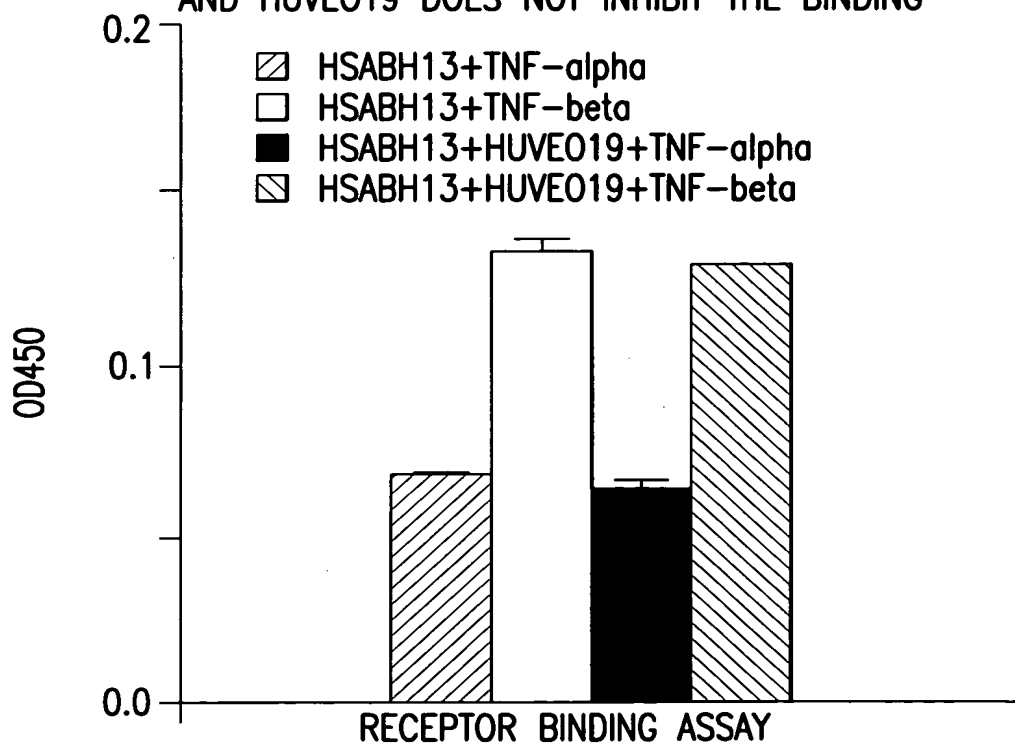


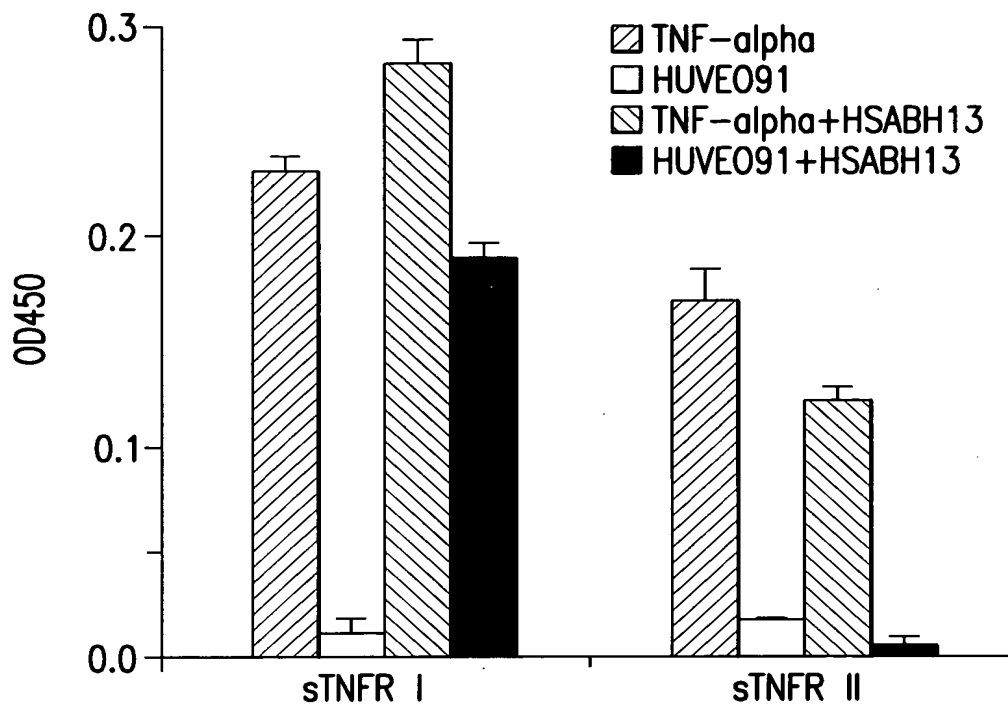
FIG.7

APPROVED	O.G. FIG.	
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DRAFTSMAN		

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HSABH13 DOES NOT COMPETE WITH sTNFR I TO BIND TNF-ALPHA,
 MAY COMPETE WITH sTNFR II TO BIND TNF-ALPHA



GOAT ANTI-HUMAN ANTIBODY TO TNFR

FIG.8

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

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TITER OF RABBIT #11509 TESTED AGAINST
 TNFr BATCH HGO2900-1-B

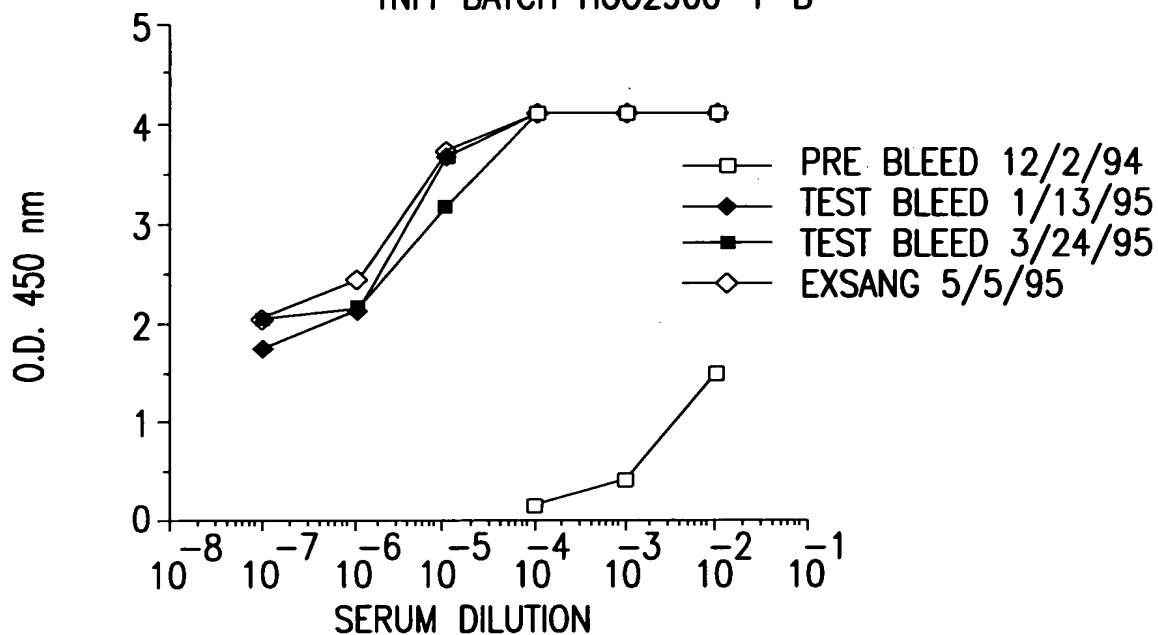


FIG. 9A

TITER OF RABBIT #11508 TESTED AGAINST
 TNFr BATCH HGO2900-1-B

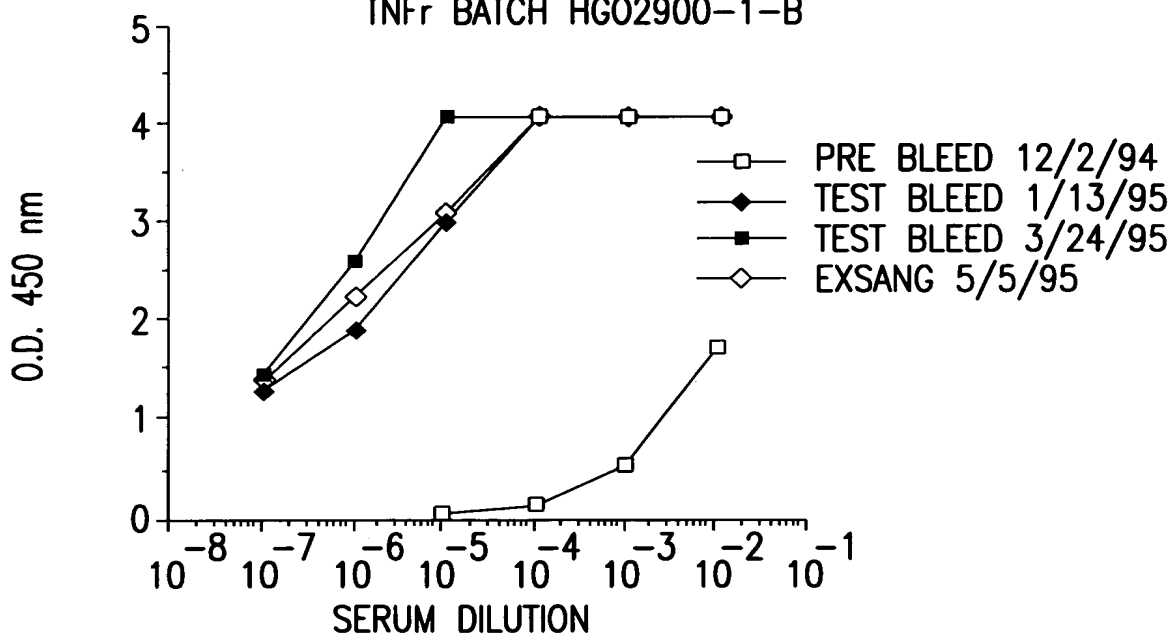


FIG. 9B